UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/426,792	10/22/99	MANGANO	D 9114-004-999

020583
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HM12/0104

EXAMINER	
SPIVACK, P	
ART UNIT	**PAPER NUMBER**
1614	9

DATE MAILED: 01/04/01

Response 7/5/01

Pleas find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/426,792	Applicant(s) Mangano
	Examiner Phyllis G. Spivack	Group Art Unit 1614

☒ Responsive to communication(s) filed on *Oct 6, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-16 and 49-51* is/are pending in the application.

Of the above, claim(s) *7-12* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6, 13-16, and 49-51* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *8*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Applicant's Amendment filed October 6, 2000, Paper No. 7, is acknowledged. Claim 52 is canceled. Claims 1-16 and 49-51 remain.

A list of references filed October 6, 2000, Paper No. 8, is further acknowledged and has been reviewed.

In Paper No. 3 the species atenolol was elected without traverse. Claims 7-12 remain withdrawn from consideration by the Examiner as being drawn to non-elected inventions, 37 CFR 1.42(b).

It is noted the recitation in dependent claim 50 "or is undergoing current vascular surgery" lacks antecedent basis in claim 1. Claim 1 is directed to a method for reducing complications *after* surgery.

In the last Office Action claims 1-6, 13-16 and 49-52 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite with respect to the recitations of heart rate and blood pressure, respectively, "greater than or equal to 65 bpm" and "greater than or equal to 100 mm Hg", the term "or" in claim 49 and missing language in claim 52.

Applicant's argument that one of skill in the art would understand the bounds of the heart rate and blood pressure is found persuasive.

Applicant has changed the term "and" in original claim 49, Paper No.3, to "or" in Paper No. 7. Applicant is requested to make this change formally.

Claim 52 is canceled.

The rejection of record under 35 U.S.C. 112, second paragraph, is maintained only with respect to claim 49.

Claims 1-6, 13-16 and 49-52 were rejected in the last Office Action under 35 U.S.C. 103 as being unpatentable over Goldstein et al., J. Cardiovascular Pharmacology. (The article in its entirety is enclosed.) It was asserted Goldstein teaches the administration of a therapeutic dose of the β_1-selective blocking agent atenolol to patients following cardiac-related surgery. Atenolol decreased both heart rate and blood pressure. Administration continued postoperatively for up to 10 days.

Applicant argues Goldstein fails to teach or suggest every element of the subject claims with respect to limitations of heart rate, blood pressure, dosages, dosing regimens and the absence of congestive heart failure, third degree block or bronchospasm. Further, Applicant urges there is a long felt need for guidelines for perioperative assessment and management of risk of coronary artery disease. Exhibit 1, Palda et al., Ann. Intern. Med., 1997, and Exhibit 2, Mangano et al., The New England Journal of Medicine, December 5, 1996, are provided as support for a long felt need.

Applicant's arguments have been given careful consideration but are not found persuasive. The terms "maximum effective dose", "conservative dose" and "aggressive dose" are used in Applicant's argument while independent claims 1 and 49 recite "near the maximum effective dose" or "about one half of the maximum effective dose". These terms are relative and would reasonably vary with respect to different patient populations concerning age, weight and renal

status. Accordingly, the 50 mg oral dose disclosed by Goldstein may be a "near maximum effective dose" or "about one half the maximum effective dose" depending on the particular patient.

The conversion of a medicament from oral dosing to intravenous -and the reverse - is conventional. The determination of an appropriate intravenous dose of atenolol when a patient is to be converted to or from oral dosing is a parameter well within the purview of those skilled in the art. It would have been reasonable to expect immediate, postoperative drug administration to be intravenous. See the top of column 2, page 254, where Goldstein states atenolol treatment was started 2 hours after extubation.

A review of the entire article, as opposed to the abstract, shows the elimination of any patient with bronchospasm, bradycardia, atrioventricular conduction defects, heart failure or recent myocardial infarction. See lines 4-10, column 2, page 254. As required by claims 15 and 16, patients suffering from coronary artery disease and those at risk for coronary artery disease were included. Although Goldstein's patient population all underwent coronary artery bypass, the parameters measured following atenolol administration are also monitored in non-cardiac related surgery. See Figures 1-3. See Table 2 where the heart rate before atenolol administration is 90.3 +/- 3.3, which meets the requirement of "greater than or equal to 65 bpm" in claims 1 and 49.

Exhibits 1 and 2 are references that were published after the filing date of the present invention. Further, according to Applicant's heading on page 8, Paper No. 7, these references are

directed to the field of management of perioperative risk of coronary artery disease. Instant claims 1 and 49 are directed to methods for reducing complications after surgery.

The rejection of record under 35 U.S.C. 103 is maintained.

No claim is allowed.

Kataria et al., J. Cardiothoracic Anesth., is cited to show the state of the art with respect to the intravenous administration the beta-adrenergic blocker esmolol to reduce cardiovascular disease complications after general surgery wherein the patient had a systolic blood pressure greater than 100 mm Hg and a heart rate greater than 65 bpm. Matangi et al., Canadian Journal of Cardiology, is further cited to show both the oral and intravenous administration of atenolol in the immediate postoperative period for the prophylaxis of postoperative arrhythmias following coronary artery bypass.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number (703) 308-4703.

December 29, 2000

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER